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## FORMULATION AND DEVELOPMENT OF LOSARTAN NANOSPONGE CAPSULES

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### ABSTRACT

The Aim of this work is to the development and evaluation of Nanosponges drug delivery system of Losartan by using solvent evaporation method. Losartan is a BCS class II drug, having a half-life of 1.5-2.5 hours, which wasn't suitable for maintaining constant plasma concentrations. So Losartan was formulated as a Nanosponge formulation for effective drug release. FTIR spectroscopy is used to identify organic, polymeric and inorganic materials of the drug in these nanosponges. Scanning electron microscopy used to identify the spherical nature of the nanosponge in all variations. The formulation F9 has better results than remaining formulations. F9 formulation shows entrapment efficiency 97.02%, drug release 98.15% in 12 hour, and follows zero order with super case II transport mechanism.

### KEYWORDS

Losartan, Nanosponges, FTIR spectroscopy, SEM disease.

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### INTRODUCTON

Nanosponges are porous polymeric delivery systems that are small spherical particles with large porous surface. The name itself suggest that these sizes are ranges from 250 nanometer to 1 micro meter in diameter. Generally nanosponges are used in targeting of cosmetic agents to skin, these are incorporated in topical systems to produce prolonged release of medicament from dosage forms and it also helps skin retention thus decreasing the discrepancy in absorption of drug, toxicity and improving patient compliance by prolonging dosing intervals. The outer surface is typically porous, allowing sustain release of drug. They are mostly use for topical drug delivery. Size range of nanosponge is 50nm-100nm<sup>1</sup>. This technology is being used in cosmetics, over-the-counter skin care, sunscreens and prescribed drugs.

Conventional formulation of topical drugs accumulates excessively in epidermis and dermis. Nanosponge prevents the accumulation of active ingredient in dermis and epidermis. Nanosponge system reduce the irritation of effective drug without reduce their efficacy<sup>2</sup>. They can be used for targeting drugs to specific sites, prevent drug and protein degradation. These tiny sponges can circulate around the body until they encounter the specific target site and stick on the surface and began to release the drug in a controlled and predictable manner<sup>3</sup>. It is possible to control the size of nanosponge. To varying the portion of cross-linkers and polymers, the nanosponge particles can be made larger or smaller<sup>4</sup>. These particles are capable of carrying both lipophilic and hydrophilic substances and of improving the solubility of poorly water soluble molecules<sup>5</sup>. Nanosponges are non-irritating, non-mutagenic, non-allergenic and non-toxic<sup>6</sup>. Nanosponges are tiny mesh-like structures that used for the treatment of many diseases and this technology is five times more effective at delivering drugs for breast cancer than conventional methods. The nanosponges are solid in nature and can be formulated as oral, parenteral, topical or inhalational dosage forms. For oral administration, these may be dispersed in a matrix of excipients, diluents, lubricants and anticaking agents which is suitable for the preparation of tablets or capsules<sup>6</sup>. For parenteral administration, these can be simply mixed with sterile water, saline or other aqueous solutions<sup>7</sup>. For topical administration, they can be effectively incorporated into topical hydrogel<sup>8</sup>. Topical nanosponge can be more patient compliant and provide sufficient patient benefits by reducing repeated doses and side effects<sup>9</sup>.

*Losartan* is an oral medication that belongs to a class of drugs called angiotensin receptor blockers (ARBs).

**Methods of preparation:** generally four methods are used to prepare nanosponges.

Solvent method, Ultra-sound assisted synthesis, Emulsion solvent diffusion method, Loading of drug into nanosponges. In this research *Losartan* nanosponges are developed by using solvent method.

**Solvent method:** in this method, Nano sponges are prepared by mixing polar aprotic solvents like

Dimethyl sulfoxide (DMSO), Dimethylformamide (DMF) with the polymer. A crosslinker is then added to this mixture in the ratio of 1:4. The above reaction should be proceeded at temperature 10°C to reflux the temperature of the solvent for the time ranging from 1 to 48 h. Once the reaction has completed, the solution is cooled down at room temperature and then obtained a product is added to bi-distilled water. The product is recovered by filtering the product under vacuum and refining by soxhlet extraction with ethanol followed by drying. Materials are used in the preparation of nanosponges: polymers, co-polymers and crosslinkers.

**Polymers examples:** Hyper cross-linked polystyrenes, cyclodextrine and its derivatives like methyl  $\beta$ -cyclodextrine, 2-hydropropyl  $\beta$ -cyclodextrine.

**Co-polymers examples:** Ethyl cellulose (EC), polyvinyl alcohol (PVA).

**Cross-linkers:** Di-phenyl Carbonate (DPC), diarylcarbonate, diisocyanates, pyromellitic anhydride, carbonyl diimidazole, 22-bis (acrylamide) acidic acid and dichloromethane<sup>8,9</sup>.

## MATERIAL AND METHODS

### Pre-formulation studies:<sup>10-17</sup>

Prior to the development of nanosponge dosage form, it is essential that certain fundamental physical and chemical properties of the drug molecule alone and when combined with excipients are determined. This first learning phase is known as pre-formulation. The main aim of the Preformulation studies are to develop information helpful to the researcher for developing safe, stable and efficacious product.

The goals of pre-formulation studies are:

- To evaluate the drug substance analytically and determine its necessary characteristics, and
- To establish its compatibility with different excipients.

### Spectroscopic study:

#### Identification of pure drug:

**Solubility studies:** Solubility of *Losartan* was carried out in different solvents like- distilled 0.1N HCL, 7.4 pH buffer and 6.8 pH buffer, and also in organic solvents like Ethanol, Methanol. Solubility studies were performed by taking excess amount of

drug indifferent beakers containing the solvents. The mixtures were shaken for 24hrs at regular intervals. The solutions were filtered by using whattmann's filter paper grade no.41. The filtered solutions were analyzed spectrophotometrically.

**Determination of absorption maximum ( $\lambda_{max}$ ):** Most drugs absorb radiation in ultraviolet region (190-390nm), as they are aromatic or contain double bonds. Accurately weighed 10mg Losartan separately was dissolved in 10 ml of methanol in a clean 10ml volumetric flask. The volume was made up to 10ml with the same which will give stock solution-I with concentration 1000 $\mu$ g/ml. From the stock solution-I, 1ml was pipette out in 10ml volumetric flask. The volume was made up to 10ml using 6.8 pH buffer to obtain stock solution-II with a concentration 100 $\mu$ g/ml. From stock solution-II, 1ml was transferred into 10ml volumetric flask. The volume was made up to 10ml using 6.8 pH buffer to get a concentration of 10 $\mu$ g/ml. This solution was then scanned at 200-400nm in UV-Visible double beam spectrophotometer to attain the absorption maximum ( $\lambda$ -max).

**Construction of calibration curve using 6.8pH buffer:**

Accurately weighed 10mg Losartan was dissolved in methanol taken in a clean 10ml volumetric flask. The volume was made up to 10ml with 6.8 pH buffer which gives a concentration of 1000 $\mu$ g/ml. From this standard solution, 1ml was pipette out in 10ml volumetric flask and volume was made up to 10ml using 6.8 pH buffer to obtain a concentration of 100 $\mu$ g/ml. From the above stock solution, aliquots of 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2 ml each was transferred to a separate 10ml volumetric flask and solution was made up to 10ml using 6.8 pH buffer to obtain a concentration of 2, 4, 6, 8, 10 and 12 $\mu$ g/ml respectively and then evaluate the absorbance of standard stock solutions by using UV spectrophotometer at 230 nm.

**Construction of calibration curve using 0.1N HCL:**

Accurately weighed 10mg Losartan was dissolved in methanol taken in a clean 10ml volumetric flask. The volume was made up to 10ml with 0.1N HCl which gives a concentration of 1000 $\mu$ g/ml. From this standard solution, 1ml was pipette out in 10ml volumetric flask and volume was made up to 10ml

using 0.1N HCl to obtain a concentration of 100 $\mu$ g/ml. From the above stock solution, aliquots of 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2 ml each was transferred to a separate 10ml volumetric flask and solution was made up to 10ml using 0.1N HCl to obtain a concentration of 2, 4, 6, 8, 10 and 12 $\mu$ g/ml respectively. The absorbance of stock solutions were measured by using UV spectrophotometer at 230 nm. The above method was repeated by using 6.8 pH phosphate buffer.

**Drug and excipient compatibility study:**

The drug and excipient compatibility was observed using Fourier Transform – Infra Red spectroscopy (FT-IR). The IR spectra showed neither shift nor disappearance of characteristic peaks suggesting that there was no interaction between drug and excipients used for the preparation of nanosponges.

**METHODOLOGY**

**Method of Preparation of Nanosponges by solvent Evaporation method:** Nanosponges are prepared by using different proportions of  $\beta$ -cyclodextrin, HP  $\beta$ -cyclodextrin, as rate retarding polymer and co-polymers like polyvinyl alcohol were prepared by solvent evaporation method (Table No.1, 2, 3). Disperse phase consisting of Losartan and requisite quantity of PVA dissolved in 10 ml solvent (methanol) was slowly added to a definite amount of PVA in 40ml of aqueous continuous phase, prepared by using magnetic stirrer. There action mixture was stirred at 1000 RPM on a magnetic stirrer for 2hours and kept on hot plate up to complete removal of organic solvent from the formulation. Then the mixture is filtered and collect filtrate and dried. The dried filtrate represents nanosponges of Losartan.

**Evaluation parameters of Nanosponges:** The Nanosponges was evaluated for various parameters:-

Entrapment Efficiency, Scanning Electron Microscopy, Particles Size and Shape, *In-Vitro* Drug Release Studies and Drug Release Kinetics Studies.

**Entrapment efficiency:** The 25mg of the Losartan weight equivalent nanosponge suspension was analysed by dissolving the sample in 10 ml of methanol. 10ml of clear supernatant liquid is taken and then determine the amount of drug dissolved

in water by using a UV method at 230nm (U.V Spectrophotometer). The concentration of the drug is determined with the help of calibration curve. The amount of drug inside the particles was calculated by subtracting the amount of drug in the aqueous phase of the suspension from the total amount of the drug in the nanoparticle suspension. The entrapment efficiency (%) of drug was calculated by the following equation.

$$\% \text{ of Drug entrapment} = \frac{\text{Mass of drug in nanosponge}}{\text{Mass of drug used in formulation}} \times 100$$

**Scanning electron microscopy:** The morphological features of prepared nanosponges are observed by using scanning electron microscopy at different magnifications.

**Dissolution study:** Dissolution is pharmaceutically defined as the rate of mass transfer from a solid surface into the dissolution medium or solvent under standardized conditions of liquid/solid interface, temperature and solvent composition. It is a dynamic property that changes with time and explains the process by which a homogenous mixture of a solid or a liquid can be obtained in a solvent. The test determines the time required for formulation to release percentage of drug under specified conditions.

#### **Dissolution Parameters**

Medium : 900ml, 0.1N HCL for 2hrs and 6.8pH buffer for 10hrs.

Apparatus : Basket (USP-I)

RPM : 50

Temperature : 37° C±0.5

Time Points : 1,2, 3,4,5,6,7,8,9,10,11,12 hr

**Procedure:** For the oral dosage forms the *in vitro* dissolution study must be conducted in the dissolution medium which simulate the *in-vivo* conditions (actual physiological conditions). The *in vitro* drug release studies for the prepared formulation were conducted for a period of 12 hrs using an Electro lab model dissolution tester USP Type-1 apparatus (rotating basket) set at 50 RPM and a temperature of 37± 0.5°C weight equivalent to 10mg of Losartan nanosponge was filled in capsule and kept in basket apparatus and placed in the 900ml of the medium. At specified intervals 5ml samples were withdrawn from the dissolution medium and replaced with fresh medium to keep

the volume constant. The absorbance of the sample solution was analyzed at 230nm for the presence of model drug, using a UV-Visible spectrophotometer.

#### **Modelling of Dissolution Profile:**

In the present study, data of the *in vitro* release were fitted to different equations and kinetic models to explain the release kinetics of Losartan from the matrix tablets. The kinetic models used were Zero order equation, First order, Higuchi release and

#### **Korsmeyer-Peppas models:**

#### **Kinetic Studies: Mathematical models:**

Different release kinetic equations (zero-order, first-order, Higuchi's equation and Korsmeyer-peppas equation) were applied to interpret the release rate of the drug from matrix systems for the optimized formulation. The best fit was calculated with higher correlation ( $r^2$ ).

#### **Zero-order release kinetic equation:**

Drug release does not depend up on the concentration of the dissolving species and the release of drug slowly can be represented by the following equation

$$Q_t = Q_0 + K_0t$$

Where  $Q_t$  is the amount of drug dissolved in time  $t$ ,  $Q_0$  is the initial amount of drug in the solution (most times,  $Q_0 = 0$ ) and  $K_0$  is the zero order release constant expressed in units of concentration/time. To study the release kinetics, data obtained from *in vitro* drug release studies were plotted as cumulative amount of drug released versus time.

**Application:** It is used to describe the drug dissolution of several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems, as well as tablets with less soluble drugs.

**First Order release kinetic equation:** This model explains the dissolution rate is dependent up on the concentration of the one dissolving species.

Release kinetic behaviour is represented as follows:

$$\text{Log } c_t = \text{log } c_0 - \frac{k_1t}{2.303}$$

Where  $C$  is the amount of drug dissolved at time  $t$ ,  $C_0$  is the amount of drug dissolved at zero time and  $k$  is the first order rate constant. Draw a plot cumulative percentage drug remaining vs time, it gives a straight line. Majority of pharmaceutical formulations follows first order kinetic profile.

### Higuchi model:

The first example of a mathematical model aimed to describe drug release from a system was proposed by Higuchi in 1961. This model is based on the parameters those are as follows

- Initial drug concentration in the is much higher than drug solubility;
- Drug diffusion takes place only in one dimension (edge effect must be negligible);
- Drug particles are much smaller than system thickness;
- Swelling and dissolution are negligible;
- Drug diffusivity is constant; and
- Perfect sink conditions are always attained in the release environment.

The Higuchi model is expressed by following equation

$$Q = K_H \cdot t^{1/2}$$

Where,  $K_H$  is the Higuchi dissolution constant.

The data obtained were plotted as cumulative percentage drug release versus square root of time.

### Korsmeyer-Peppas model:

Korsmeyer *et al.* (1983) derived a simple relationship which described drug release from a polymeric system equation. To find out the mechanism of drug release, first 60% drug release data were fitted in Korsmeyer-Peppas model,

$$M_t / M_\infty = Kt^n$$

Where,  $M_t / M_\infty$  is a fraction of drug released at time  $t$ ,  $k$  is the release rate constant and  $n$  is the release exponent. The  $n$  value is used to characterize different release for cylindrical shaped matrices.

In this model, the value of  $n$  characterizes the release mechanism of drug as described in the following Table No..

## RESULTS AND DISCUSSION

**Discussion:** From the above obtained solubility studies we can say solubility of the drug is more in 6.8pH buffer than the other buffers. In organic solvents the solubility was found more in methanol.

**Drug excipient compatibility:** Drug and excipient compatibility was confirmed by comparing spectra of FT-IR analysis of pure drug with that of various excipients used in the formulation.

**Discussion:** Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and excipients were studied. The characteristic absorption peaks of drug and excipients were obtained as shown above and as they were in official limits ( $\pm 100 \text{ cm}^{-1}$ ) the drug is compatible with excipients.

**Determination of absorption maximum ( $\lambda_{\text{max}}$ ):** Determination of Losartan  $\lambda_{\text{max}}$  was done in 6.8 pH phosphate buffer for accurate quantitative assessment of drug dissolution rate.

**Discussion:** The maximum absorbance of the Losartan in pH 6.8 buffer was found to be 230nm.

**Discussion:** The linearity was found to be in the range of 2-12 $\mu\text{g/ml}$  in 0.1N HCL and 6.8 phosphate buffer. The regression value was closer to 1 indicating the method obeyed Beer-lambert's law.

### A) Particle size analysis of Nanosponges:

The particle size of the nanosponge was determined by optical microscopy and the nanosponges were found to be uniform in size. The average particle size of all formulations ranges from 316.4 nm to 454.8 nm which is in increasing order due to the increase in the concentration of polymer but after certain concentration it was observed that as the ratio of drug to polymer was increased, the particle size decreased. This could probably be due to the fact that in high drug to polymer ratio, the amount of polymer available per nanosponge was comparatively less. Probably in high drug-polymer ratios less polymer amounts surround the drug and reducing the thickness of polymer wall and nanosponges with smaller size were obtained. By performing the particle size analysis, it is concluded that the formulation has the particle size varies with the concentration of polymer drug ratio.

**B) Morphology determination by scanning electron microscopy (SEM):** Scanning electron microscopy (SEM) was used to determine the Morphology of the prepared nanosponges. SEM is useful for characterizing the morphology and size of microscopic specimens with particle size as low as 10 -10 to 10 -12 grams. The sample was placed in an evacuated chamber and scanned in a controlled pattern by an electron beam. Interaction of the electron beam with the specimen produces a variety of physical phenomena that, when detected, are

used to form images and provide elemental information about the specimens.

The morphology of the nanosponges prepared by emulsion solvent evaporation method were investigated by SEM. The representative SEM photographs of the nanosponges are shown in Fig. It was observed that the nanosponges were spherical, and uniform with no drug crystals on the surface. The shape of the nanosponges affects the surface area and surface area per unit weight of spherical nanosponges. The irregular shape of the particles may affect dissolution rate present in dissolution environment. The spongy and porous nature of the nanosponges can be seen in figures.

#### **Entrapment efficiency:**

It is calculated to know about the efficiency of any method, thus it helps in selection of appropriate method of production. After the preparation of formulations the Practical yield was calculated as Nanosponges recovered from each preparation in relation to the sum of starting material (Theoretical yield). It can be calculated using following formula.

$$\text{Entrapment efficiency} = \frac{\text{Practical yield}}{\text{Theoretical yield (drug + polymer)}} \times 100$$

**Discussion:** The entrapment efficiency of formulation F1-F9 was found to be in the range of 86.59 to 101.26%.

#### **In vitro dissolution studies of prepared nanosponges:**

**In vitro** release studies were performed in triplicate using USP basket method at 50 rpm and  $37 \pm 0.2^\circ\text{C}$  in 900ml of 0.1N HCl for 2hrs and remaining hours in phosphate buffer (pH 6.8). 10 mg of the formulated nanosponges is used for each experiment. Samples were taken at appropriate time intervals for 1,2,3,4,5,6,7,8,9,10,11, and 12 hour. The samples were measured spectrophotometrically at 230nm. Fresh dissolution medium was replenished each time when sample is withdrawn to compensate the volume.

**Discussion:** From the above *in vitro* dissolution studies it was observed that the formulations containing ethylcellulose with PVA using solvent evaporation method with drug in (1:0.5, 1:1, 1:1.5).

F1 Formulations shows maximum drug release at the end of 6<sup>th</sup> hour. Whereas F2 formulation shows maximum drug release at the end of 8hr. while F3 formulation shows maximum drug release at the end of 10hr.

**Discussion:** From the above *in vitro* dissolution studies it was observed that the formulations containing  $\beta$  cyclodextrin with PVA using solvent evaporation method with drug in (1:0.5, 1:1, 1:1.5). F4 Formulations shows maximum drug release at the end of 8 hour. Whereas F5 formulation shows maximum drug release at the end of 9hr. while F6 formulation shows maximum drug release at the end of 11hr.

**Discussion:** From the above *in vitro* dissolution studies it was observed that the formulations containing HP- $\beta$  cyclodextrin with PVA using solvent evaporation method with drug in (1:0.5, 1:1, 1:1.5). F7 Formulations shows maximum drug release at the end of 9 hour. Whereas F8 formulation shows maximum drug release at the end of 11hr. while F9 formulation shows maximum drug release at the end of 12hr. By comparing the above dissolution studies of formulations F1-F9. Maximum drug release was found in F9 formulation containing Drug: HP- $\beta$  cyclodextrin in 1:1.5 ratio. So F9 formulation was taken as the optimized formulation, and drug release kinetics were performed for F9 formulation.

**Discussion:** The optimized formulation F9 has coefficient of determination ( $R^2$ ) values of 0.993, 0.827, 0.948, 0.740 for Zero order, First order, Higuchi, Korsmeyer Peppas respectively. A good linearity was observed with the Zero order, the slope of the regression line from the Higuchi plot indicates the rate of drug release through the mode of diffusion and to further confirm the diffusion mechanism, data was fitted into the Korsmeyer Peppas equation which showed linearity with n value of 1.228 for optimized formulation. Thus n value indicates the supercase II transport mechanism.

**Table No.1: Excipients used in design of Formulation**

S.No	Excipient Used	Supplier
1	Losartan	Cadila Pharmaceuticals Limited
2	$\beta$ -Cyclodextrin	B.M.R.Chemicals, Hyderabad
3	Polyvinyl alcohol (PVA)	B.M.R.Chemicals, Hyderabad
4	HP $\beta$ cyclodextrin	B.M.R.Chemicals, Hyderabad
5	Ethyl Cellulose	B.M.R.Chemicals, Hyderabad
6	Methanol	B.M.R.Chemicals, Hyderabad
7	Water	B.M.R.Chemicals, Hyderabad

**Table No.2: Equipment's used in Design Formulation**

S.No	Instruments	Sources
1	Electronic Weighing Balance	Shimadzu Corporation Tokyo, Japan
2	UV-Vis Spectrophotometer (T60)	PG Instrument
3	FTIR Spectrophotometer	Shimadzu Corporation Tokyo, Japan
4	Dissolution Apparatus	LAB India
5	Magnetic stirrer	Remi industries, Kerala

**Table No.3: Formulation table of Losartan loaded nanosponges using solvent evaporation method**

S.No	Excipients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Losartan (g)	1	1	1	1	1	1	1	1	1
2	Ethyl Cellulose (g)	0.5	1	1.5	--	--	--	--	--	--
3	$\beta$ -cyclodextrin (g)	--	--	--	0.5	1	1.5		--	--
4	HP- $\beta$ Cyclodextrin (g)	--	--	--	--	--	--	0.5	1	1.5
5	PVA (mg)	200	200	200	200	200	200	200	200	200
6	Ethanol	20	20	20	20	20	20	20	20	20
7	Water	40	40	40	40	40	40	40	40	40

**Table No.4: Drug transport mechanisms suggested based on 'n' value**

S.No	Release exponent	Drug transport mechanism	Rate as a function of time
1	0.5	Fickian diffusion	$t^{-0.5}$
2	$0.45 < n = 0.89$	Non -Fickian transport	$t^{n-1}$
3	0.89	Case II transport	Zero order release
4	Higher than 0.89	Super case II transport	$t^{n-1}$

**Table No.5: Solubility Studies of Losartan**

S.No	Buffer	Solubility ( $\mu\text{g/ml}$ )
1	0.1 N HCL	0.368
2	6.8 pH buffer	0.832
3	7.4pH buffer	0.756
4	Ethanol	1.245
5	Methanol	2.069



**Table No.6: Calibration curve data of Losartan in 0.1N HCL**

S.No	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.124
3	4	0.259
4	6	0.386
5	8	0.506
6	10	0.632
7	12	0.761

**Table No.7: Calibration curve of Losartan in 6.8 pH buffer**

S.No	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.152
3	4	0.294
4	6	0.445
5	8	0.592
6	10	0.731
7	12	0.879

**Table No.8: Entrapment Efficiency F1-F9**

S.No	Formulation code	% Entrapment Efficiency
1	F1	93.56
2	F2	86.59
3	F3	99.52
4	F4	101.26
5	F5	100.64
6	F6	93.76
7	F7	95.46
8	F8	95.61
9	F9	97.02

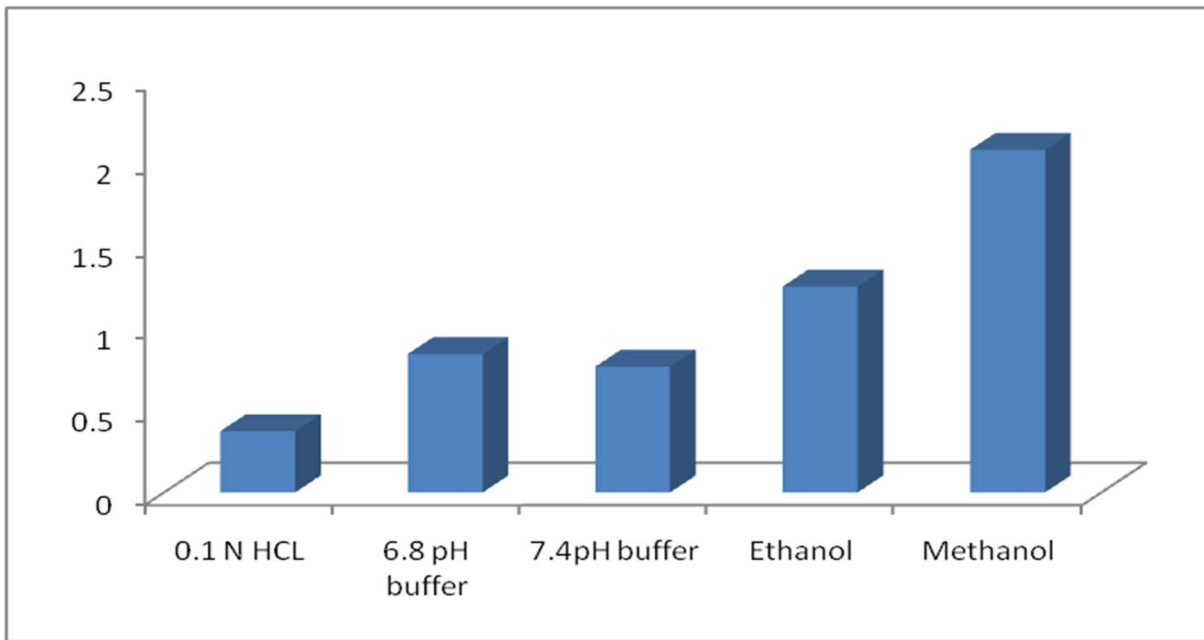
**Table No.9: Percentage of drug release of Nanosponges (F1-F9)**

S.No	Time(hrs)	% CDR								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0	0	0	0	0	0	0	0	0	0
2	1	28.65	27.64	20.49	26.45	20.59	16.52	22.36	17.84	16.59
3	2	46.21	45.2	27.49	29.76	29.36	29.52	33.46	25.63	22.64
4	3	68.28	58.34	36.45	37.46	39.16	35.96	41.52	39.42	29.63
5	4	76.25	66.15	42.79	52.65	49.79	44.53	49.19	48.22	36.49
6	5	88.94	72.42	50.64	64.21	50.95	56.28	62.61	57.24	47.25
7	6	98.61	80.94	60.63	78.28	62.59	57.83	69.32	62.84	56.19
8	7	---	89.26	70.16	86.25	72.36	65.06	76.25	70.16	62.45
9	8	---	95.12	79.27	92.51	85.19	68.03	89.32	77.24	71.61
10	9	---	---	84.36	---	95.36	76.46	96.15	82.28	79.35
11	10	---	---	95.24	---	---	86.94	---	90.52	88.24
12	11	---	---	---	---	---	96.24	---	99.64	91.52
13	12	---	---	---	---	---	---	---	---	98.15

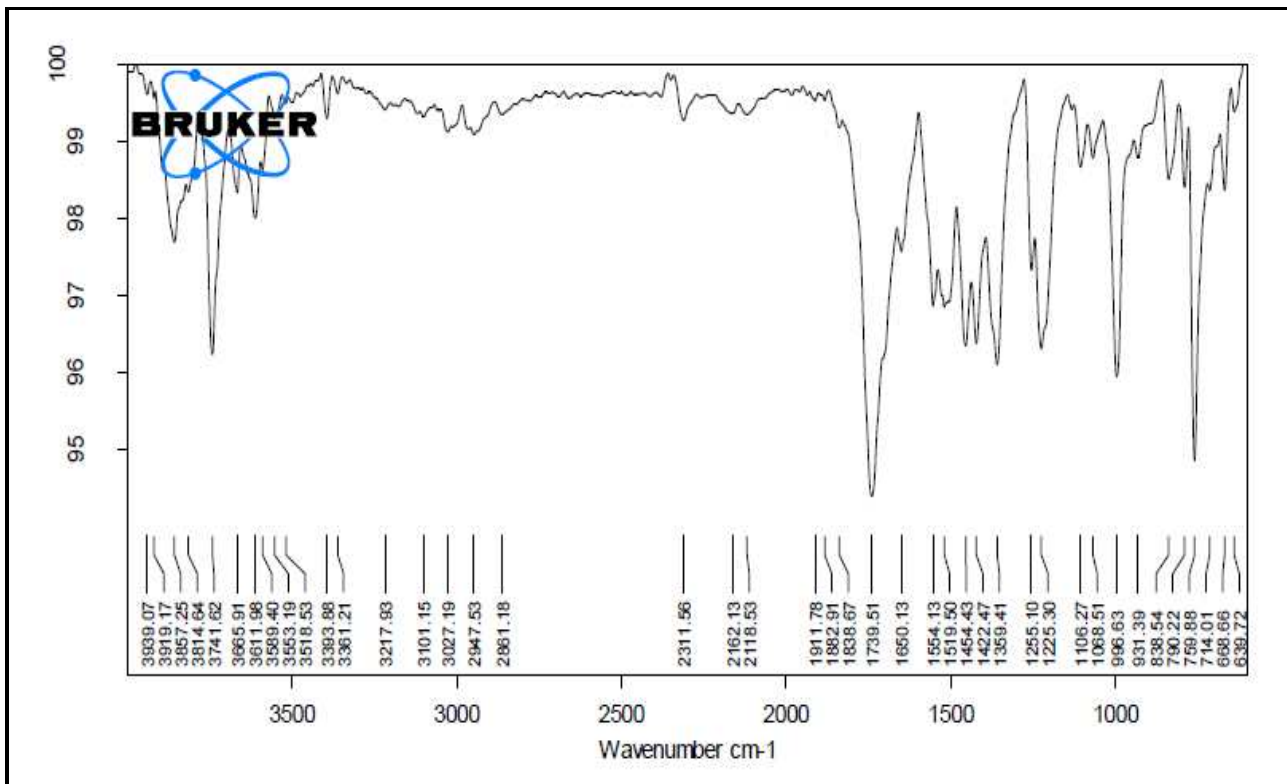


**Table No.10: Regression values**

S.No	Formulation Code	Zero order	First order	Higuchi	Peppas	Peppas
		R <sup>2</sup>	R <sup>2</sup>	R <sup>2</sup>	R <sup>2</sup>	n
1	F9	0.993	0.827	0.948	0.740	1.228



**Figure No.1: Solubility Studies of Losartan**



**Figure No.2: FTIR Spectra of Pure Drug**

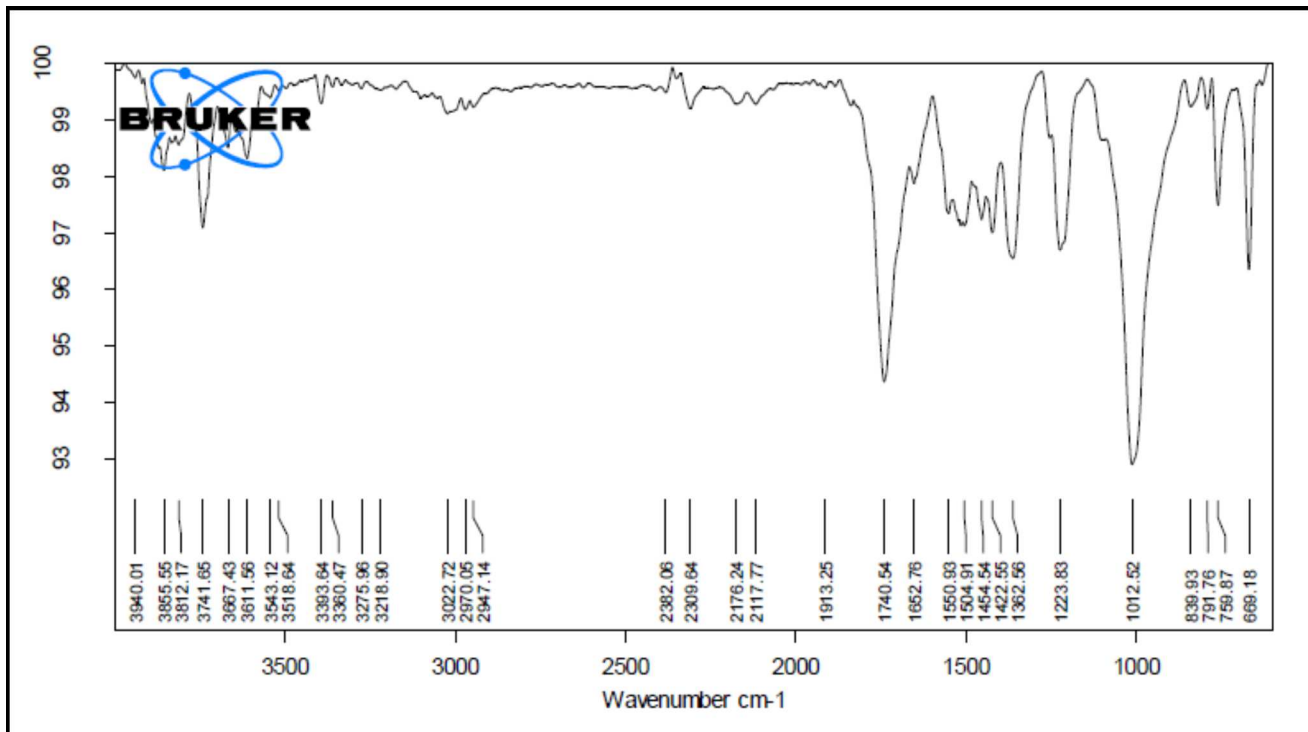


Figure No.3: FTIR Spectra of Optimized Formulation

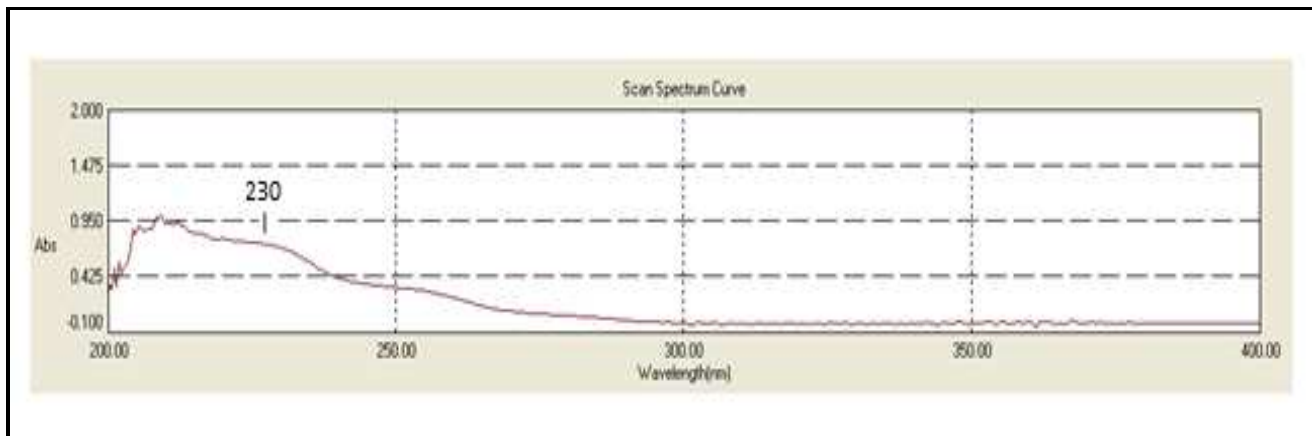


Figure No.4: λ-max in 6.8 phosphate buffer

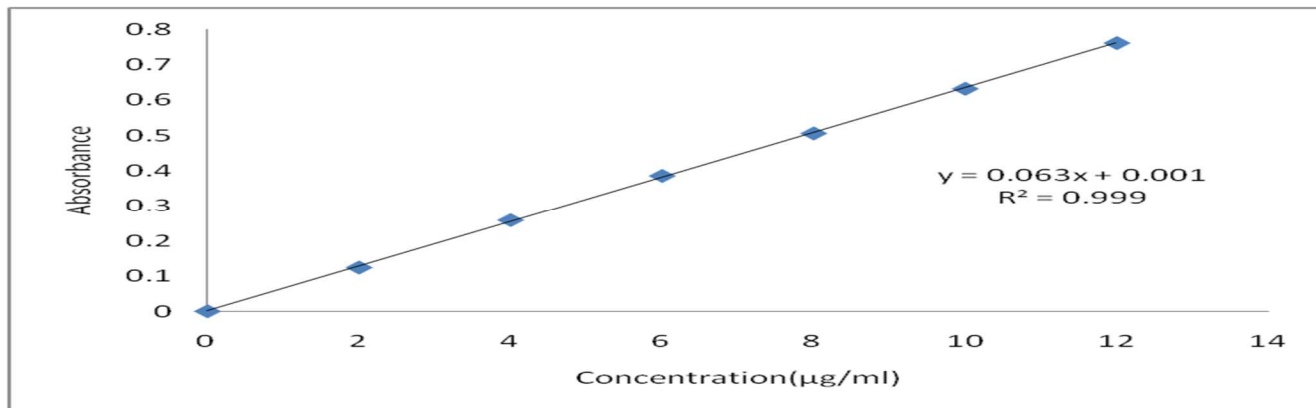


Figure No.5: Calibration curve data of Losartan in 0.1N HCL

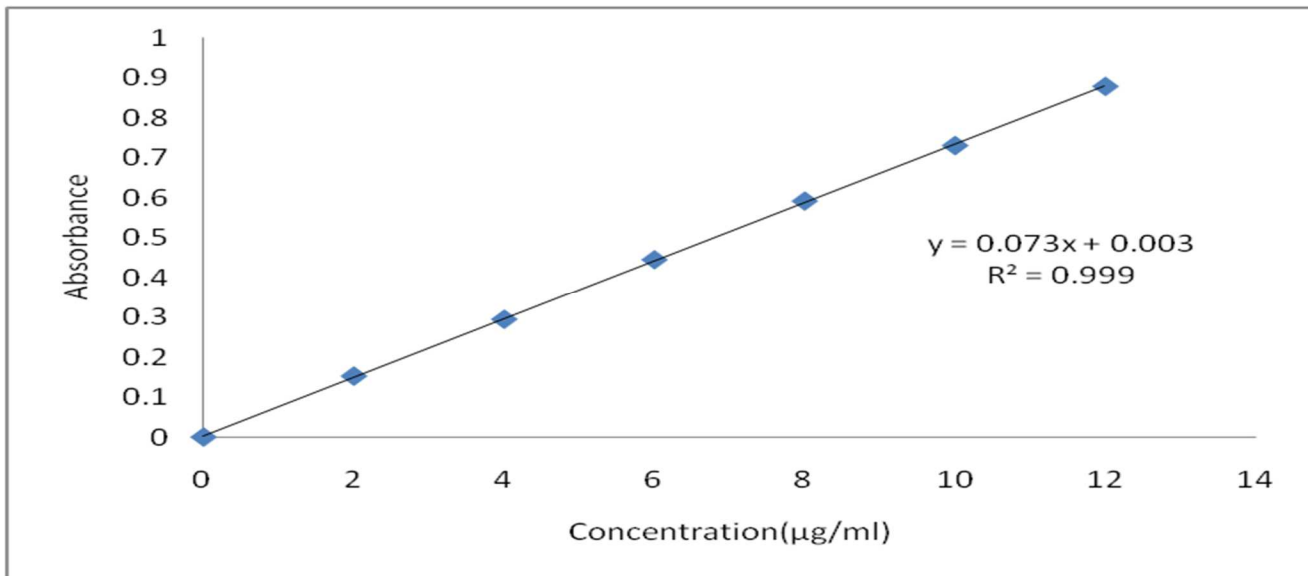


Figure No.6: Calibration curve of Losartan in 6.8 pH buffer

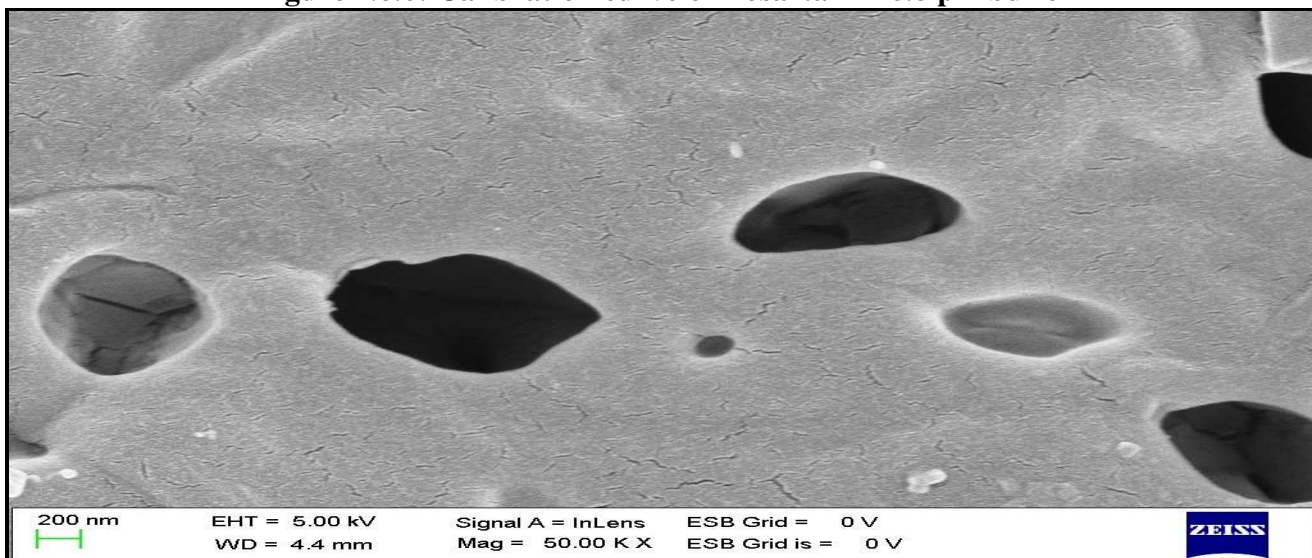


Figure No.7: Nanosponges structure optimized formulation (F9)

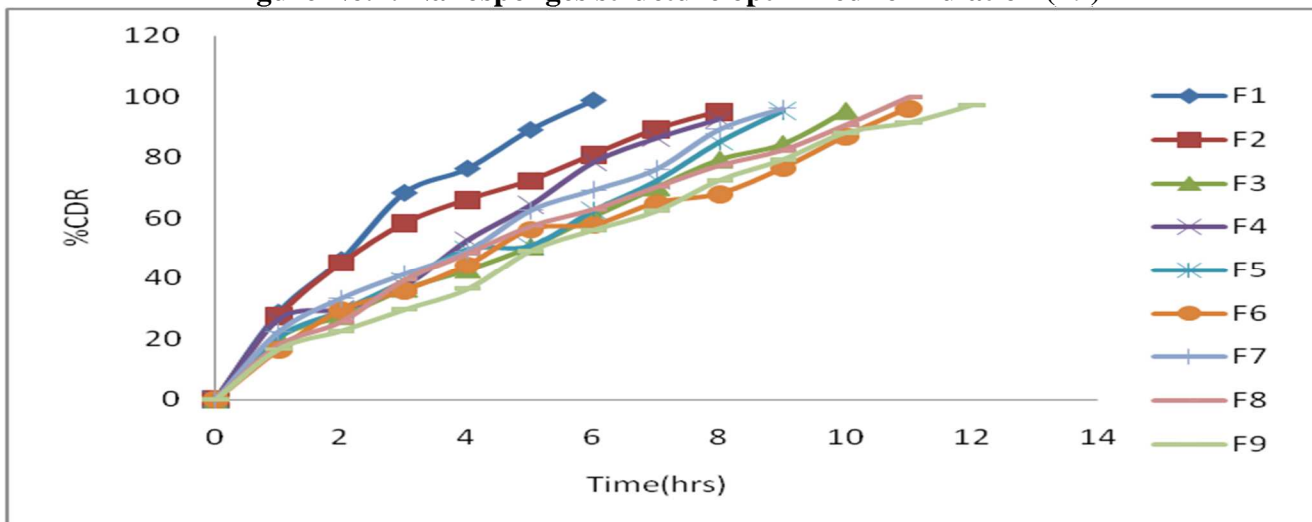


Figure No.8: Percentage cumulative drug release graph F1-F9

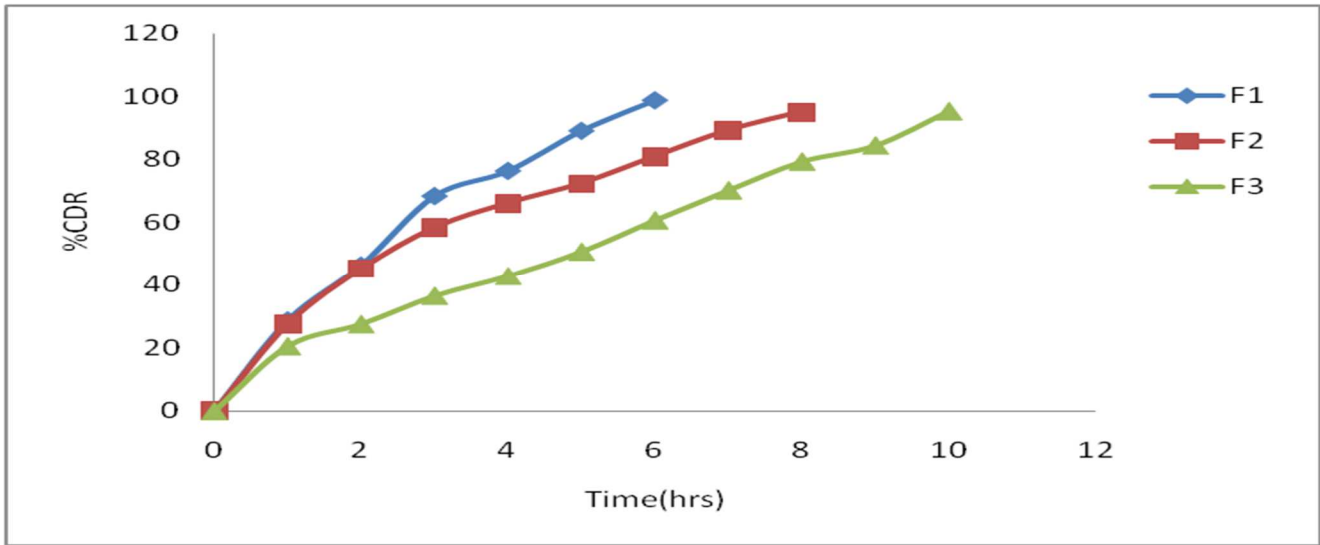


Figure No.9: Percentage of drug release graph F1-F3

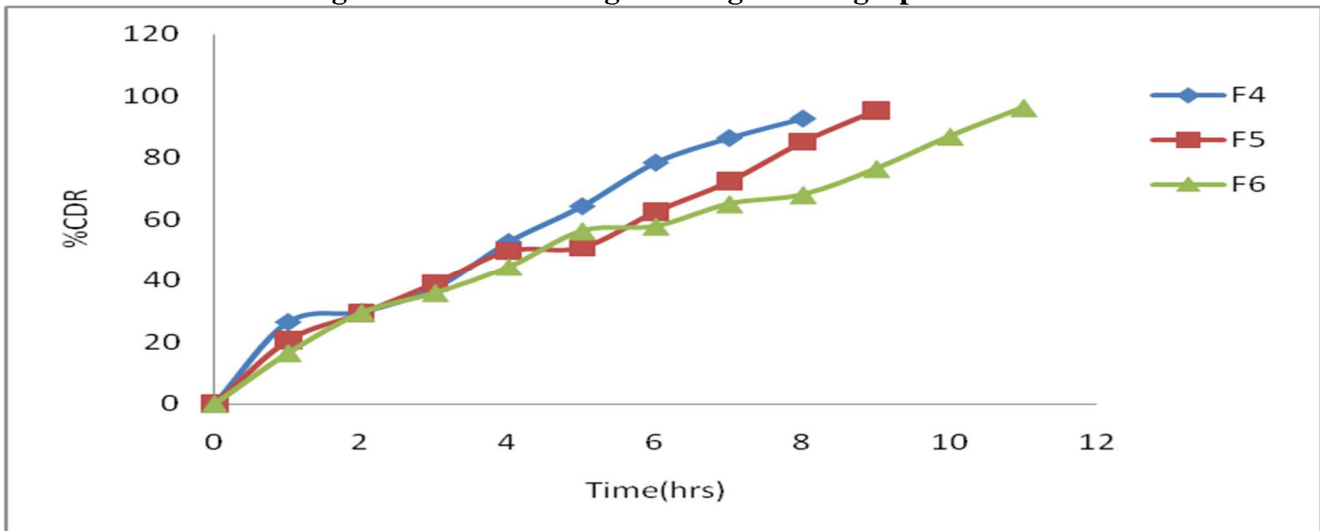


Figure No.10: Percentage of drug release graph F4-F6

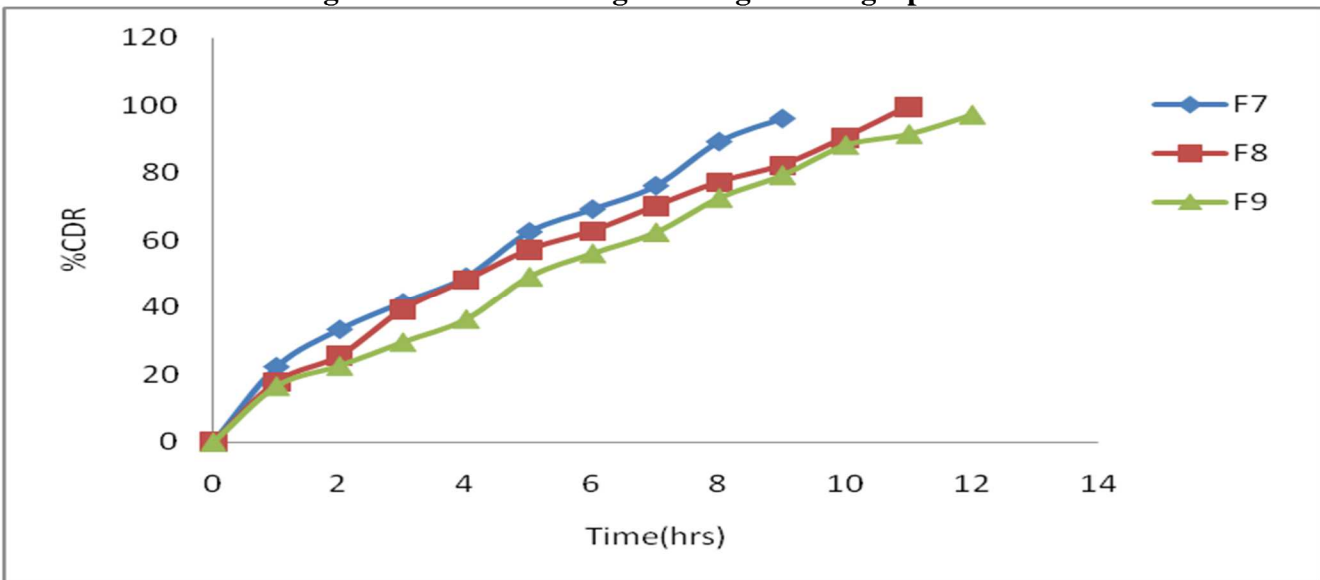


Figure No.11: Percentage of drug release graph F7-F9

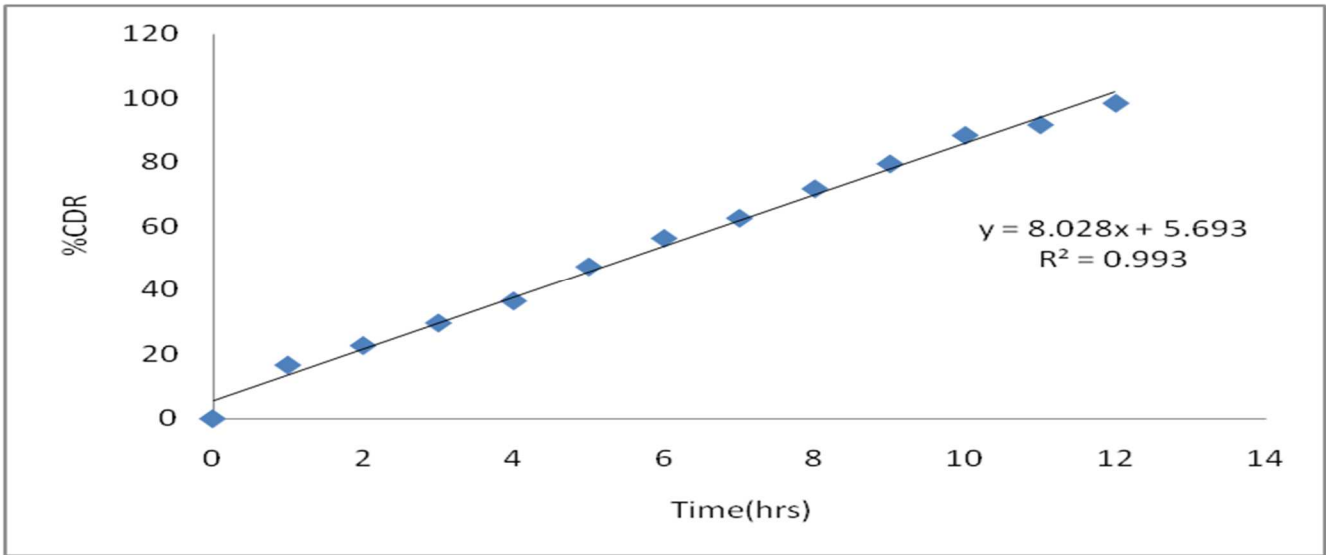


Figure No.12: Zero Order graph for F9

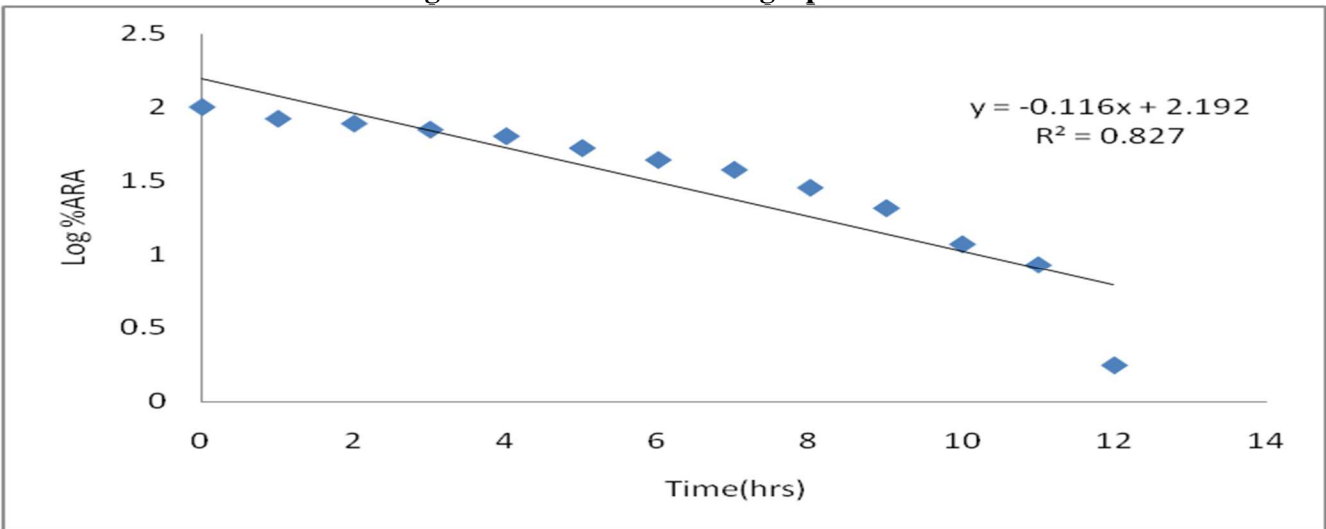


Figure No.13: First Order graph for F9

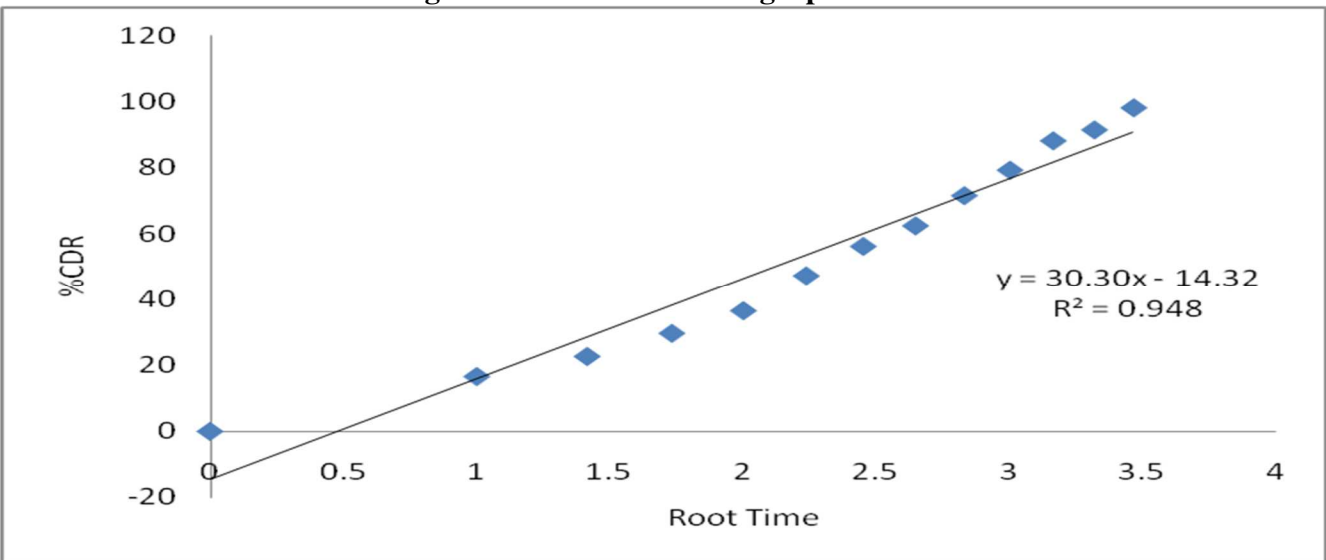


Figure No.14: Higuchi Plot for F9

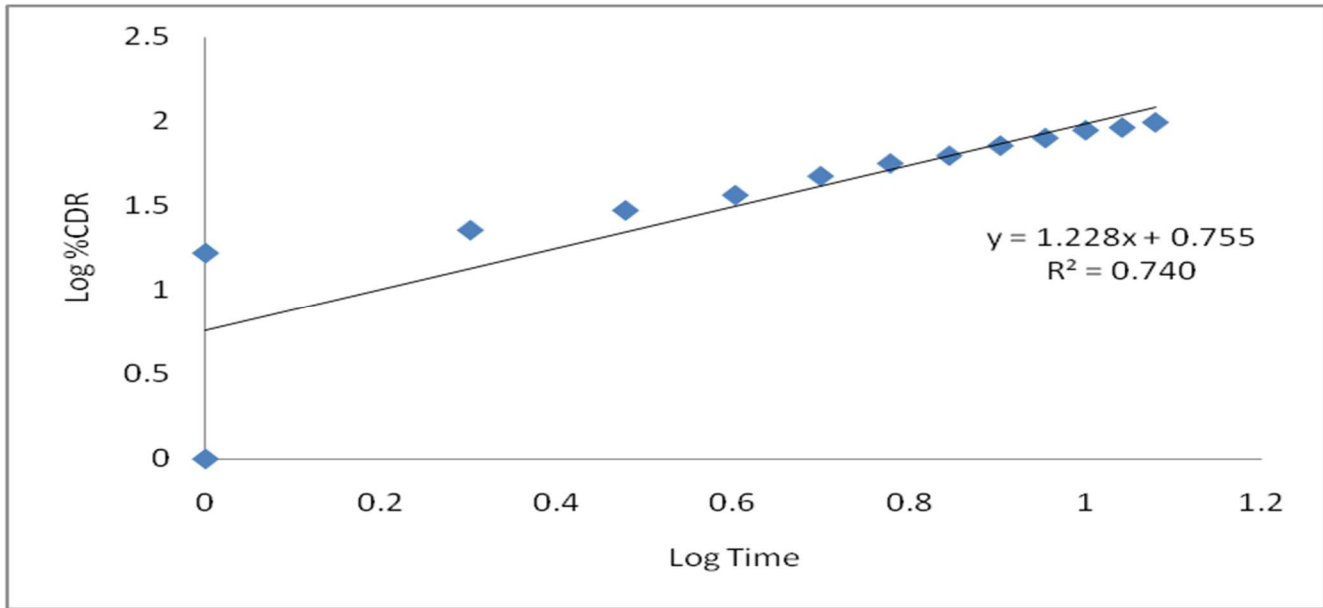


Figure No.15: Peppas Plot for F9

## CONCLUSION

The Nanosponge was prepared by solvent evaporation method using ethyl cellulose,  $\beta$  cyclodextrin and HP-  $\beta$  cyclodextrin, as rate retarding polymers, PVA and methanol as cross linking agents. The prepared nanosponges were evaluated for its different parameters which revealed many interesting results for efficient preparation of the nanosponge. FTIR spectroscopy is used to identify organic, polymeric and inorganic materials of the drug in these nanosponges. Scanning electron microscopy used to identify the spherical nature of the nanosponge in all variations. With the obtained results from various evaluation parameters, it may be concluded that nanosponge drug delivery system has become competitive, rapidly evolving technology and more researches are carried out to optimize effectiveness of cost. The formulation F9 has better results than other 9 formulations. F9 has its particle size 200nm, entrapment efficiency 97.02%, drug release 98.24 % in 12 hour, The optimized formulation F9 has coefficient of determination ( $R^2$ ) values of 0.993, 0.827, 0.948, 0.740 for Zero order, First order, Higuchi, KorsmeyerPeppas respectively. A good linearity was observed with the Zero order, the slope of the regression line from the Higuchi plot indicates the rate of drug release through the mode of diffusion and to further confirm the diffusion

mechanism, data was fitted into the Korsmeyer Peppas equation which showed linearity with n value of 1.228 for optimized formulation. Thus n value indicates the supercase II transport mechanism.

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## CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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